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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00N-1256]

Over-the-Counter Drug Products; Public Hearing

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public hearing; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is announcing a public hearing about the agency's approach to regulating over-the-counter (OTC) drug products. The purpose of the hearing is to solicit information from, and the views of, interested persons, including scientists, professional groups, and consumers. FDA intends to elicit comment on general issues regarding the status of OTC drug products, including the criteria the agency should consider in rendering decisions on OTC availability of drugs, the classes of products, if any, that are not currently available OTC that should or should not be available OTC, how FDA can be assured that consumers understand the issues relating to OTC availability of drug products, how rational treatment decisions are affected by coexisting prescription and OTC therapies for a given disease, whether the current structure for marketing OTC products in the United States is adequate, and FDA's role in switching products from prescription to OTC status.

DATES: The public hearing will be held on Wednesday, June 28, and Thursday, June 29, 2000, from 8:30 a.m. to 4:30 p.m. Submit written notices of participation and comments for consideration at the hearing by June 2, 2000. Written comments will be accepted after the hearing until August 25, 2000.

ADDRESSES: The public hearing will be held at the Gaithersburg Holiday Inn, 2 Montgomery Village Ave., Gaithersburg, MD 20879. Submit written notices of participation to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061,

Rockville, MD 20852; email: FDADockets@oc.fda.gov; or through the Internet at <http://www.accessdata.fda.gov/scripts/oc/dockets/meetings/meetingdocket.cfm>. Submit comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852; email: FDADockets@oc.fda.gov; or through the Internet at <http://www.accessdata.fda.gov/scripts/oc/dockets/comments/commentdocket.cfm>. Transcripts of the hearing will be available for review at the Dockets Management Branch (address above) and on the Internet at <http://www.fda.gov/ohrms/dockets>.

FOR FURTHER INFORMATION CONTACT: Patricia L. DeSantis, Center for Drug Evaluation and Research (HFD-2), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-594-5400, e-mail: desantis@cder.fda.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA regulates all prescription and OTC drug products marketed in the United States. Section 503(b) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 353(b)) describes the criteria for determining whether a drug product is subject to prescription classification. Under section 503(b)(1) of the act, a drug requires a prescription if:

(A) because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, [it] is not safe for use except under the supervision of a practitioner licensed by law to administer such drug; or

(B) [it] is limited by an approved application under section 505 [of the act] to use under the professional supervision of a practitioner licensed by law to administer such drug.

All drug products not meeting the above criteria may be sold OTC.

In 1972, FDA initiated rulemaking procedures (the OTC Drug Review) to determine which OTC drugs can be generally recognized among qualified experts as safe and effective and not misbranded under prescribed, recommended, or suggested conditions of use. Through the OTC

Drug Review, FDA establishes monographs for classes of OTC drug products (e.g., antacids, skin protectants) that are found to be generally recognized as safe and effective and not misbranded when the products contain the ingredients and are labeled according to the monograph. OTC drug monographs describe the active ingredients, amount of drug, formulation, labeling, and other general requirements for drugs to be lawfully sold OTC.

The regulations for the OTC Drug Review are found in part 330 (21 CFR part 330) and the monographs are in 21 CFR parts 331 through 358. The regulations set forth standards for safety, effectiveness, benefit-to-risk considerations, and labeling of OTC drug products.

The standards for safety, effectiveness, and labeling for OTC products are described in § 330.10(a)(4). Safety for OTC use means a low incidence of adverse reactions or significant side effects under adequate directions for use and warnings against unsafe use, as well as low potential for harm which may result from abuse under conditions of widespread availability. Effectiveness means a reasonable expectation that, in a significant proportion of the target population, the pharmacological effect of the drug, when used under adequate directions for use and warnings against unsafe use, will provide clinically significant relief of the type claimed. The benefit-to-risk ratio of a drug must be considered in determining both safety and effectiveness.

The labeling of OTC drug products must be clear and truthful in all respects and may not be false or misleading in any particular. The labeling must state: (1) The intended uses and results of product use; (2) the adequate directions for proper use; and (3) the warnings against unsafe use, side effects, and adverse reactions in terms that render them likely to be read and understood by the ordinary individual, including individuals of low comprehension, under customary conditions of purchase and use (§ 330.10(a)(4)(v)).

During the course of the OTC Drug Review, advisory review panels of nongovernment experts evaluated the various classes of OTC drug products and recommended that a number of drugs be switched from prescription to OTC status. FDA acted on these recommendations and switched a number of products to OTC status, including antihistamines (e.g., diphenhydramine hydrochloride

(HCl), doxylamine succinate), topical nasal decongestants (e.g., oxymetazoline HCl, xylometazoline HCl), topical hydrocortisone, topical antifungals (e.g., haloprogin, miconazole nitrate), an anthelmintic (pyrantel pamoate), an oral anesthetic (dyclonine HCl), and various fluoride dental rinses.

FDA has also approved the switch of a number of drugs from prescription to OTC status under new drug applications. These include an antidiarrheal (loperamide), topical antifungals (e.g., clotrimazole, terbinafine HCl), antihistamines (e.g., clemastine fumarate), a pediculicide (permethrin), an ocular vasoconstrictor (oxymetazoline HCl), vaginal antifungals (e.g., clotrimazole, miconazole nitrate), analgesics (e.g., ketoprofen, naproxen sodium), acid reducers (e.g., cimetidine, famotidine), a hair growth treatment (minoxidil), and smoking cessation drugs (e.g., nicotine polacrilex).

In allowing these drugs to be sold OTC, the agency considered the safety and effectiveness criteria stated above, the benefit-to-risk ratio, and whether clear and understandable labeling could be written for self-medication without the intervention of a health professional. In some cases, manufacturers were required to conduct labeling comprehension studies to determine if consumers would understand the proposed OTC labeling for the products.

FDA has received comments in the past suggesting that a number of other types of drugs should be considered for OTC status. These types of products include diuretics, antihypertensive agents, cholesterol-lowering drugs, antidiabetic drugs, treatments for osteoporosis, topical agents for the treatment of perioral herpetic lesions, drugs for problems of the stomach and intestines, asthma treatments, and oral contraceptives.

Drugs found appropriate for OTC sale have an increasingly vital role in the U.S. health care system by providing consumers easy access to certain drugs that can be used safely for conditions that consumers can self-treat without the help of a health care practitioner. Consumers have access to more than 100,000 OTC drug products encompassing more than 800 active ingredients and covering more than 100 therapeutic categories or classes.

In light of the continuously changing health care environment, including the growing self-care movement, the agency continues to examine its overall philosophy and approach to regulating OTC drug products. FDA is soliciting information from, and the views of, interested persons, including health professional groups, scientists, industry, and consumers, on the agency's regulation of OTC drug products.

II. Scope of the Hearing

The regulation of OTC drug products raises many complex public health issues. To promote a more useful discussion at the public hearing, FDA has developed a list of questions and issues. This list is not intended to be exclusive, and presentations and comments on other issues related to the development and regulation of OTC drugs are encouraged. Issues that are of specific interest to the agency include the following:

A. Criteria

- In the context of the present environment, what criteria should FDA consider in rendering decisions on OTC availability of drug products?
- What types of drugs are or are not appropriate for OTC distribution?
- What types of diseases are or are not suitable for treatment with products marketed OTC (e.g., chronic illnesses; diseases that require initial diagnosis by a physician; diseases that if left untreated, or are inadequately treated, can lead to serious morbidity or mortality)?
- How should the risks and benefits to individuals and risks and benefits to the public health be assessed and weighed in any decision on OTC marketing? For example, how should the agency balance the potential benefits of OTC antimicrobial agents with the potential risks to society at large of the development of resistant organisms associated with increased, and potentially improper, use?

B. Classes of Products

- Are there specific classes of products that are not currently marketed OTC that should be available OTC? If so, which ones and why? What specific evidence should be required to support such approvals?
- Are there specific classes of products that should not be available OTC? What specific concerns do these classes raise?

Examples of specific classes that might be discussed in brief include: Diuretics, antihypertensive agents, cholesterol-lowering drugs, oral antidiabetic agents, treatments for osteoporosis (including its prevention), antimicrobials, and oral contraceptives.

C. Consumer Understanding

- How can FDA be assured of consumer understanding of the benefits and risks of specific drug products and the ability of consumers to use products safely and effectively were the drug products to be marketed OTC? Issues that may be discussed include: (1) Sampling criteria for comprehension studies; (2) language barriers; (3) appropriate use and interpretation of self-administered diagnostic tests; (4) ramifications of misdiagnosis; (5) ability of consumers to appreciate, without required intervention by a physician, the need for continuous (sometimes life-long) treatment, appropriate followup, and need for other treatment; (6) consumer confusion between trade names and generic/chemical names; and (7) consumer confusion with brand extensions (e.g., when the active ingredients generally associated with a brand are not present in some of the brand's extended product line).

- What methodologies can be employed to demonstrate consumer understanding?
- How can information on efficacy be adequately conveyed to consumers through labeling?

For example, how can the label adequately convey this efficacy information for: (1) Therapies with marginal benefit or (2) therapies with preventive claims that may provide benefit to a specific population but the benefit to the individual consumer is unclear?

- Can prevention claims encourage ill-advised behavior, and if so, how could this potential be minimized? For example, would use of a cholesterol-lowering drug allow patients to ignore other needed interventions such as smoking cessation, dietary discretion, and management of other risk factors?

D. Selection of Treatment

- With regard to the choice of treatment regimens, how can rational selection be ensured when there are coexisting prescription and OTC therapies for a given disease?

- In an environment with coexisting products, what are the most effective means to ensure that patients know the best ways to treat their illnesses?

- How should the availability of OTC options and prescription options for the same indication be reconciled? Are there examples where this dichotomy would raise public health concerns?

- Within a therapeutic class, should the first drug to enter the OTC market be the “best” drug, in terms of the benefit-to-risk ratio? How should the availability of a “better” OTC product, in terms of efficacy or safety, affect the status of products already on the OTC market for treatment of the same condition? Should older therapies that may provide less benefit or more risk be removed from the OTC market, or should the labeling be revised? Suppose the more effective drug is more difficult to use and must remain prescription—might that encourage use of the less satisfactory drug?

E. OTC Marketing System

- Is the current structure for marketing OTC products in the United States adequate? What lessons can we learn from different OTC marketing systems? For example, what can be learned from the countries and those U.S. states where some nonprescription drug products are sold OTC and others are sold “behind the counter”?

F. FDA's Role in Switches

- Under what circumstances should FDA actively propose OTC marketing for a drug in the absence of support from the drug sponsor?
- Should FDA be more active in initiating switches of prescription products to OTC use?

III. Notice of Hearing Under 21 CFR Part 15

The Commissioner of Food and Drugs (the Commissioner) is announcing that the public hearing will be held in accordance with part 15 (21 CFR part 15). The presiding officer will be the Commissioner or her designee. The presiding officer will be accompanied by a panel of Public Health Service employees with relevant expertise.

Persons who wish to participate in the part 15 hearing must file a written notice of participation with the Dockets Management Branch (address above) prior to June 2, 2000. To ensure timely handling, any outer envelope should be clearly marked with the Docket No. 00N-1256 and the statement "FDA Regulation of OTC Drug Products Hearing." Groups should submit two copies. The notice of participation should contain the person's name; address; telephone number; affiliation, if any; the sponsor of the presentation (e.g., the organization paying travel expenses or fees), if any; brief summary of the presentation; and approximate amount of time requested for the presentation. The agency requests that interested persons and groups having similar interests consolidate their comments and present them through a single representative. FDA will allocate the time available for the hearing among the persons who file notices of participation as described above. If time permits, FDA may allow interested persons attending the hearing who did not submit a written notice of participation in advance to make an oral presentation at the conclusion of the hearing.

After reviewing the notices of participation and accompanying information, FDA will schedule each appearance and notify each participant by telephone of the time allotted to the person and the approximate time the person's oral presentation is scheduled to begin. The hearing schedule

will be available at the hearing. After the hearing, the hearing schedule will be placed on file in the Dockets Management Branch under Docket No. 00N-1256.

Under § 15.30(f), the hearing is informal, and the rules of evidence do not apply. No participant may interrupt the presentation of another participant. Only the presiding officer and panel members may question any person during or at the conclusion of each presentation.

Public hearings under part 15 are subject to FDA's policy and procedures for electronic media coverage of FDA's public administrative proceedings (part 10, subpart C (21 CFR part 10, subpart C)). Under § 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants. The hearing will be transcribed as stipulated in § 15.30(b). The transcript of the hearing will be available on the Internet at <http://www.fda.gov/ohrms/dockets> and orders for copies of the transcript can be placed at the meeting or through the Freedom of Information Staff (HFI-35), 5600 Fishers Lane, Rockville, MD 20857.

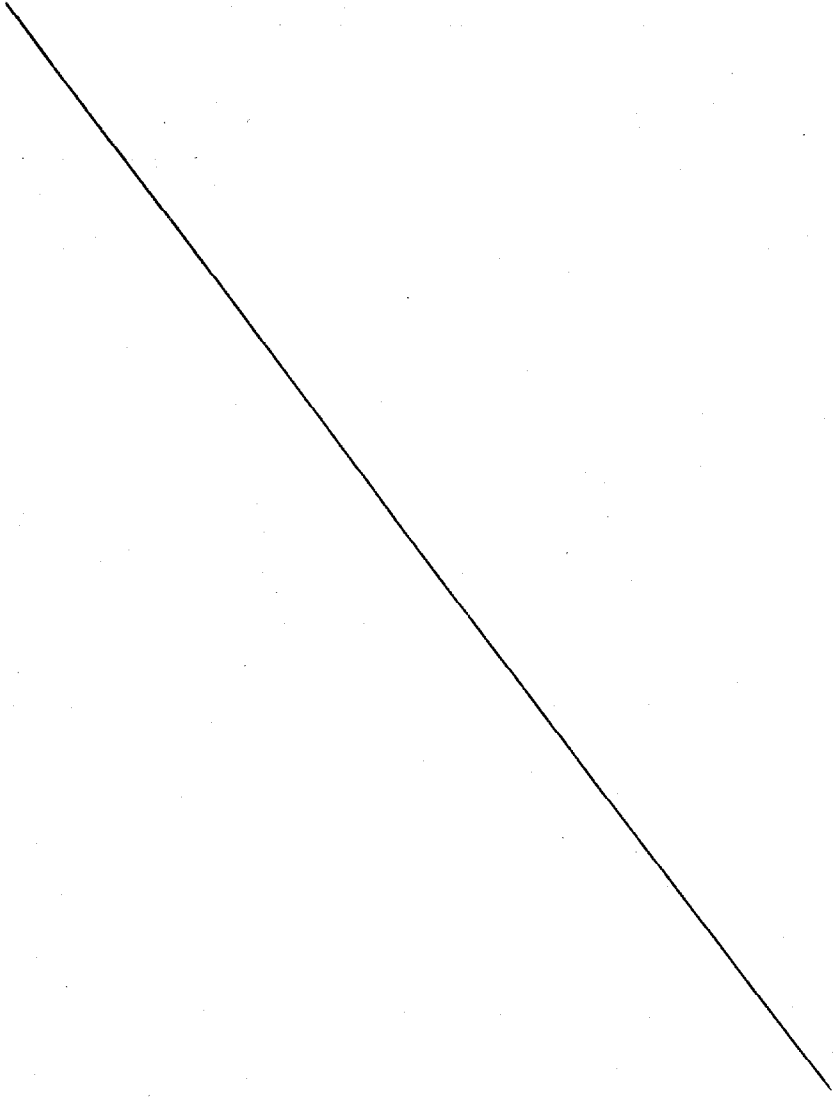
Any handicapped persons requiring special accommodations to attend the hearing should direct those needs to the contact person listed above.

To the extent that the conditions for the hearing, as described in this notice, conflict with any provisions set out in part 15, this notice acts as a waiver of those provisions as specified in § 15.30(h).

IV. Request for Comments

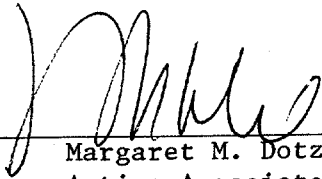
Interested persons may submit to the Dockets Management Branch (address above) written notices of participation and comments for consideration at the hearing by June 2, 2000. To permit time for all interested persons to submit data, information, or views on this subject, the administrative record of the hearing will remain open following the hearing until August 25, 2000. Persons who wish to provide additional materials for consideration should file these materials

with the Dockets Management Branch (address above) by August 25, 2000. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with



the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: 4/17/00
April 17, 2000



Margaret M. Dotzel
Acting Associate Commissioner for Policy

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